

**CLAIMS:**

1. A method for capturing biological particles, comprising:  
 contacting a capture system with biological particles under  
 conditions whereby the biological particles bind to the capture system,  
 5 wherein:  
     the capture system comprises a plurality of addressed loci;  
     the capture system comprises an addressed collection of  
 polypeptide-tagged molecules bound to addressed capture agents at each  
 locus;  
 10 the capture agents at each locus bind to the same polypeptide tag;  
     the polypeptide tag to which the capture agent binds is different  
 among the loci; and  
     each locus in capture system contains a plurality of different  
 molecules each with the same tag bound to the capture agents at the  
 15 locus.
2. The method of claim 1, wherein the polypeptide tags are  
 evenly distributed among the tagged molecules such that the diversity of  
 tagged molecules at each locus in the capture system is within one order  
 of magnitude.
- 20 3. The method of claim 2, wherein the diversity of tagged  
 molecules among the loci is within 0.5 order of magnitude.
4. The method of claim 2, wherein the diversity of tagged  
 molecules among the loci is within 0.1 order of magnitude.
5. The method of claim 2, wherein the diversity of tagged  
 25 molecules among the loci is within 0.05 or 0.01 order of magnitude.
6. The method of claim 1, wherein the tagged molecules have a  
 diversity of at least about  $10^2$ ,  $10^3$ ,  $10^4$ ,  $10^5$ ,  $10^6$ ,  $10^7$ ,  $10^8$ ,  $10^9$ ,  $10^{10}$ ,  
 $10^{11}$  or  $10^{12}$ .
7. The method of claim 2, wherein the biological particles are  
 30 selected from the group consisting of cells, portions of cells, cell

membranes, viruses, viral capsids, viral particles, bacterial cells, subcellular compartments, organelles and micells.

8. The method of claim 7, wherein the biological particles are selected from the group consisting of prokaryotic cells, eukaryotic cells,  
5 intracellular particles, nuclei, cell membranes, cell membrane fragments, nuclear membranes, nuclear membranes fragments, viral vectors or viral capsids with or without packaged nucleic acid, phage, phage vectors, phage capsids with or without encapsulated nucleotide acid, liposomes and other micellar agents.
- 10 9. The method of claim 1, wherein the tagged molecules comprise tagged polypeptides or tagged nucleic acid molecules.
10. The method of claim 1 wherein the tagged molecules comprise tagged antibodies or fragments thereof.
11. The method of claim 10, wherein the tagged molecules  
15 comprise scFvs.
12. The method of claim 1, wherein the tagged molecules comprise a library of molecules.
13. The method of claim 12, wherein the library is an antibody library or a library of nucleic acid molecules encoding an antibody library.
- 20 14. The method of claim 12, wherein the library is an scFv library or a nucleic acid library encoding the scFvs.
15. The method of claim 1, wherein the capture agents comprise polypeptides or nucleic acids or analogs thereof.
16. The method of claim 1, wherein the capture agents comprise  
25 receptors, ligands, drugs, enzymes, or enzymes that are modified to have altered catalytic activity.
17. The method of claim 1, wherein the capture agents comprise antibodies or fragments thereof.
18. The method of claim 1, wherein the capture system  
30 comprises a positionally addressable array.

19. The method of claim 18, wherein the capture agents are immobilized at discrete loci on a solid support.

20. The method of claim 19, wherein the solid support is selected from the group consisting of silicon, celluloses, metal, polymeric  
5 surfaces, radiation grafted supports.

21. The method of claim 19, wherein the solid support is selected from the group consisting of gold, nitrocellulose, polyvinylidene fluoride (PVDF), radiation grafted polytetrafluoroethylene, polystyrene, glass and activated glass.

10 22. The method of claim 19, wherein the support comprises a wells or pit or plurality thereof in the surface.

23. The method of claim 1, wherein the capture agents are addressed by linking or association with electronic, chemical, optically or color-coded labels.

15 24. The method of claim 23, wherein the labels comprise particulate supports.

25. The method of claim 24, wherein the particulate support is selected from the group consisting of silicon, celluloses, metal, polymeric surfaces and radiation grafted supports.

20 26. The method of claim 24, wherein the particulate support is selected from the group consisting of gold, nitrocellulose, polyvinylidene fluoride (PVDF), radiation grafted polytetrafluoroethylene, polystyrene, glass and activated glass.

25 27. The method of claim 1, wherein each locus in the capture system further comprises a secondary agent or plurality thereof at one or more loci, wherein:

the second agents are common to a plurality of loci;  
bind to and/or interact with the captured biological particles; and  
each of the plurality are the same or different.

30 28. The method of claim 27, wherein a plurality of different second agents are added.

29. The method of claim 27, wherein the amounts of the second agents vary from locus to locus.

30. The method of claim 27, wherein the second agents are selected from the group consisting of antibodies known to bind to the  
5 captured biological particles, adhesion molecules, drugs, receptors, enzymes and combinations thereof.

31. The method of claim 27, where the second agent serves to anchor the biological particle, to act as a co-stimulatory molecule, to bind to surface receptors different from the capture agents, to exert a  
10 biological effect, or to further select the biological particles that bind to a locus.

32. The method of claim 27, wherein the second agent is selected from the group consisting of trastuzumab and rituximab.

33. The method of claim 1, wherein the biological particles are  
15 cells selected from the group consisting of immune cells, neurons, cancer cells, bacterial cells and infected cells.

34. The method of claim 1, wherein the biological particles are subcellular compartments, organelles, viral particles or pathogens.

35. The method of claim 33, wherein the cells are dendritic cells,  
20 T cells, or B cells.

36. The method of claim 1, further comprising:  
assessing the effects of capture on a biological particle or plurality thereof.

37. The method of claim 36, wherein the effect is detected by  
25 visualizing the captured biological particles or wherein the effect is detected by staining captured biological particles or portions thereof.

38. The method of claim 1, further comprising:  
detecting or identifying the captured biological particles.

39. The method of claim 38, wherein identification is effected by  
30 staining or visualizing captured biological particles.

40. The method of claim 1, wherein the biological particles are labeled prior to capture.

41. The method of claim 1, further comprising: identifying tagged molecules that capture the biological particles.

5        42. The method of claim 40, further comprising: identifying tagged molecules that capture labeled biological particles.

43. The method of claim 1, wherein the biological particles are cells that comprise a reporter gene construct that comprises a transcriptional regulatory region whose activity is modulated by  
10 interaction of a protein in or on the cell with a modulator of the activity of the protein.

44. The method of claim 1, further comprising detecting molecules or biological particles by specifically staining or by visualizing captured molecules or biological particles.

15        45. The method of claim 44, wherein the stain specifically reacts with a one or a plurality of the captured molecules or biological particles.

46. The method of claim 44, wherein a plurality of stains are applied.

20        47. The method of claim 46, wherein one stain reacts with a feature common to all molecules or biological particles of a particular type, and at least one other stain reacts with a subset thereof.

48. The method of claim 44, wherein the stains are selected from the group consisting of fluorescent dyes, luminescent labels, enzyme labels and immunostains.

25        49. The method of claim 44, wherein the stains are selected from the group consisting of green fluorescent protein, red fluorescent protein, blue fluorescent protein, an immunostain and semiconductor crystals.

30        50. The method of claim 1, wherein contacting is performed in the presence and absence of a test compound, and the results are compared to identify test compounds that alter binding of biological

particles to the capture system or an activity or property of the biological particles.

51. The method of claim 1, further comprising:  
adding a test compound or exposing the capture system to a  
5 condition before, during or after contacting the capture system with the biological particles; and after contacting assessing the effects of the test compound on the biological particles that are captured or on the pattern of captured biological particles.

52. A method of identifying molecules that interact with  
10 infectious agents, comprising:  
a) performing the method of claim 1, wherein the biological particles comprise infectious agents; and  
b) identifying the tagged molecules that interact with the infectious agents.

- 15 53. A method for profiling the surface of a biological particle comprising:  
a) performing the method of claim 1; and  
b) identifying the tagged molecules that interact with the biological particle, thereby developing a binding profile of molecules on  
20 the surface of the biological particle.

54. The method of claim 53, further comprising:  
adding a test compound or exposing the capture system to a condition before, during or after contacting the capture system with the biological particles; and  
25 assessing the effect(s) of the test compound or condition on the profile.

55. A method for identifying a modulator of an interaction among proteins in a biological particle, comprising:  
a) performing the method of claim 1;

b) adding a test compound or exposing the capture system to a condition before, during or after contacting the capture system with the biological particles, and

c) identifying a change in an interaction of the biological  
5 particles with the capture system or a change in the captured biological particles to thereby identify a molecule that modulate protein interactions in or on the biological particle.

56. The method of claim 55, wherein the change is assessed by detecting a change in binding pattern or a physical or chemical change in  
10 the biological particles or is a conformational change in a protein or proteins in or on the biological particle.

57. The method of claim 56, wherein the protein interaction mediates signal transduction, or the protein interaction is an association interaction, or protein interaction is a dissociation interaction.

15 58. The method of claim 55, wherein test compound modulates the degradation of a biopolymer in the biological particles.

59. The method of claim 55, wherein the biopolymer is selected from the group consisting of an oligonucleotide, an oligonucleoside, a polypeptide, a peptide nucleic acid, a carbohydrate, a lipid, a  
20 polysaccharide and derivatives and combinations thereof.

60. A method of identifying a molecule that modulates the trafficking in biological particles, comprising:

a) performing the method of claim 1;  
b) monitoring trafficking in the biological particle,  
25 to thereby identifying the molecule from among the tagged molecules that modulate trafficking in the biological particle.

61. The method of claim 60, wherein the tagged molecules or test compounds are selected from the group consisting of enzymes, proteins, receptors, cellular adhesion molecules, antibodies and fragments  
30 thereof.

62. A method of identifying a molecule that modulates trafficking in biological particles, comprising:

- a) performing the method of claim 1;
- b) adding a test compound or exposing the capture system to a  
5 condition before, during or after contacting the capture system with the biological particles; and
- c) monitoring trafficking in the biological particle, to thereby identify the test compound and/or condition that modulates trafficking in the biological particle.

10 63. The method of claim 62, wherein the tagged molecules or test compounds are selected from the group consisting of enzymes, proteins, receptors, cellular adhesion molecules, antibodies and fragments thereof.

15 64. A method for identifying a molecule that modulates an activity or a functional or structural property in or of the biological particles, comprising:

- a) performing the method of claim 1;
- b) adding a test compound or exposing the capture system to a  
20 condition before, during or after contacting the capture system with the biological particles; and
- c) monitoring the activity, function or structural property in or of the biological particles, to thereby identifying the molecules and/or conditions from among the test compounds or test conditions that modulates the activity, function or structural property.

25 65. The method of claim 64, wherein the activity, function or structural property is selected from the group consisting of proliferation, apoptosis, morphology, transcription, translation, receptor internalization, receptor shedding, signal transduction, receptor-mediated activation of a biological particle, receptor-activated signaling in a biological particle,  
30 differentiation, dedifferentiation, interactions among constituent proteins and/or protein complexes and components thereof, interactions among



biological particles, endocytosis, phagocytosis, exocytosis, phosphorylation, dephosphorylation and change in kinetics of an intra-particle reaction.

5 66. A method of mapping epitopes of molecules displayed on the surface of a biological particle, comprising:

- a) performing the method of claim 1, wherein the capture system displays libraries of tagged molecules that comprise potential ligands for proteins or molecules on the surface of the biological particle;
  - b) identifying tagged molecules that interact with the biological particles, thereby compiling a epitope map of the biological particle.
- 10

67. The method of claim 66, wherein the tagged molecules comprise a library of T-cell receptors.

68. The method of claim 66, wherein the captured biological particles are antigen presenting cells (APCs).

15 69. The method of claim 68, wherein the APCs are recombinant cells modified to express peptides in the context of the major histocompatibility complex (MHC, class I or class II) on their surfaces.

70. The method of claim 1, further comprising:  
optionally separating the unbound biological particles from the bound particles;

20

detecting or identifying loci to which biological particles bind or to which biological particles that exhibit an altered phenotype or altered structure or activity, to thereby identify tags; and

based upon the tags from the loci to which the biological particles have bound, identifying the tagged molecules.

25

71. A method of sorting biological particles, comprising:  
a) performing the method of claim 1;  
b) separating the unbound biological particles from the bound particles, thereby sorting the biological particles to reduce the diversity thereof.

30

72. The method of claim 71, further comprising detecting or identifying loci to which biological particles bind to thereby identify tags.

73. The method of claim 72, based upon the tags from the loci to which the biological particles have bound, identify the tagged  
5 molecules.

74. A method of identifying a receptor on the surface of biological particles that transduces a signal from a polypeptide, comprising:

- a) performing the method of claim 1;
- 10 b) identifying the biological particles in which an extracellular signal is transduced, thereby identifying the locus and tag bound to the locus;
- c) identifying a molecule linked to the tag, to thereby identify the molecule that binds to cell surface receptor and transduce the signal.

15 75. The method of claim 74, further comprising identifying the receptor on the surface of biological particles that interacts with the identified molecule.

20 76. A method for identifying a molecule that interacts with an apically-localized molecule on a biological particle, comprising:

- a) performing the method of claim 1;
- b) separating unbound biological particles from bound biological particle(s); and
- c) identifying the molecule that interacts with the bound  
25 biological particle(s), thereby identifying the molecule that interacts with the apically-localized molecule.

77. The method of claim 76, wherein the biological particles are selected from the group consisting of cells, portions of cells, cell membranes, viruses, viral capsids, viral particles, bacterial cells,  
30 subcellular compartments, organelles and micells.

78. A method for identifying molecules that modulate an activity or a functional or structural property in or of the biological particles, comprising:

- a) performing the method of claim 1;
- 5        b) monitoring the activity, the function or structural property in or of the biological particles, to thereby identifying the molecules from among the tagged molecules that modulate the activity, function or structural property.

79. The method of claim 78, wherein the activity, function or  
10 structural property is selected from the group consisting of proliferation, apoptosis, morphology, transcription, translation, receptor internalization, receptor shedding, signal transduction, receptor-mediated activation of a biological particle, receptor-activated signaling in a biological particle, differentiation, dedifferentiation, interactions among constituent proteins  
15 and/or protein complexes and components thereof, interactions among biological particles, endocytosis, phagocytosis, exocytosis, phosphorylation, dephosphorylation and change in kinetics of an intra-particle reaction.